A PATCH FOR THE CONTROLLED DELIVERY OF COSMETIC, DERMATOLOGICAL, AND PHARMACEUTICAL ACTIVE INGREDIENTS INTO THE SKIN

Background of the Invention

1. Field of the Invention

The present invention relates to a patch for the controlled delivery of cosmetic, dermatological, and pharmaceutical active ingredients onto the skin which is formed of a single polymeric matrix layer. Upon application to the skin surface, the patch provides a substantive therapeutic layer to the treatment site over an extended period of time.

2. Description of the Related Art

The localized treatment of body tissues, diseases, and wounds requires that the particular active ingredient be maintained at the site of treatment for an effective period of time. Transdermal patches for the administration of active ingredients onto the skin have become very popular in recent years. These patches adhere to the targeted area and the active ingredient is continually absorbed through the skin into the bloodstream for systemic distribution.

The term "transdermal" as used herein, means transdermal or percutaneous administration, i.e. application of the skin treating composition directly to the skin to be treated. Hence the terms "skin," "derma," "epidermis," and the like shall also be used interchangeably unless specifically stated otherwise.

Transdermal patches, which permit the controlled release of the active ingredients onto the skin, are known from the literature. Two types of patches for skin applications are described in the literature. The first type of patches has a multilayer structure, where the active ingredients are dissolved or dispersed in the various layers. The second type of patch is a pressure-sensitive adhesive patch, where the active is dissolved or dispersed in the patch adhesive layer. Multilayer patches normally have a structure comprising several successive layers in the following order: a first support layer, which is typically

occlusive, such as, composed of a material impermeable to the active compound, so as to prevent the evaporation thereof and facilitate transdermal migration; a second storage layer fastened to the support layer and containing the active compound and capable of placement directly in contact with the skin; a layer of an adhesive material applied to the surface of the storage layer and permeable to the active compound to facilitate attachment of the patch to the skin; and a detachable protective layer which hermetically covers the storage layer so as to protect it from any external contamination during storage prior to use of the patch. In the pressure sensitive adhesive patches, the bioactive substances are mixed with and formulated into a pressure sensitive adhesive matrix which may be subsequently coated as a single pressure sensitive adhesive layer.

U.S. Patent No. 6,280,764 discloses a patch for topical application of an anti-acne formulation has in various embodiments a backing film, a release layer and at least one adhesive polymeric matrix layer located between the backing film and the release layer. The anti-acne formulation is uniformly distributed throughout one or more polymeric matrix layers and has an anti-acne effective amount of at least two agents selected from the group of an anti-microbial, an antiseptic, an anti-irritant, a keratolytic agent, a hormone, a hormone agonist and a hormone antagonist.

U.S. Patent No. 6,296,869 discloses a dermal patch which includes a substrate formed of a hydrophobic and hydrophilic fiber mixture, and a hydrogel adhesive deposited onto the substrate. The adhesive contains an alpha or beta hydroxy acid. The patch is applied to skin for treating the signs of aging, especially around areas of the eye.

U.S. Patent No. 6,280,765 discloses patch comprising a hydrophobic polymer layer bound to a support layer and containing: a) first particles of at least one water-soluble active compound, b) second particles of oil, c) at least one liposoluble active compound, d) third particles of a water-absorbing agent all of which are dispersed homogeneously in the polymer layer. This patch allows the packaging and controlled administration of an assembly of skin-nourishing and/or skin-repairing substances of different nature, and also has excellent adhesive power on the skin.

U.S. Patent No. 5,232,702 describes a patch structure consisting of an occlusive support layer and a polymer layer bound to the support layer. The polymer layer is formed of a matrix of a silicone polymer including, in the dispersed state, fatty substances

and hydrophilic active compounds. This form of patch is more particularly suitable for delivering water-soluble active compounds of lipophilic nature.

U.S. Patent No. 5,976,565 discloses a patch for topical application of an anti-acne formulation has in various embodiments a backing film, a release layer and at least one adhesive polymeric matrix layer located between the backing film and the release layer. The anti-acne formulation is uniformly distributed throughout one or more polymeric matrix layers and has an anti-acne effective amount of at least two agents selected from the group consisting of an anti-microbial, an antiseptic, an anti-irritant, a keratolytic agent, a hormone, a hormone agonist and a hormone antagonist.

U.S. Patent No. 5,100,672 discloses a pressure sensitive adhesive transdermal patch having a composite adhesive layer reinforced with a web layer. Cosmetically bioactive substances used in the patch include water soluble vitamins such as vitamin C, and liposoluble vitamins A and E or their derivatives.

U.S. Patent No. 6,180,133 discloses an anti-wrinkle skin treating composition comprises a pressure sensitive matrix patch having dissolved in the adhesive a mixture of antioxidants in the form of a vitamins C ester and vitamin E. Also preferably dissolved in the adhesive are glycerine and a polydiorganosiloxane adhesion-adjusting agent. Optionally dissolved in the adhesive is also one or more members selected from the group consisting of moisturizing agents, skin collagen synthesis promoting agents and exfoliating agents. When applied to a wrinkled skin area the composition acts to diminish fine wrinkles and improves the overall thickness, elasticity, firmness and smoothness of the skin. The modified adhesive properties of the patch are sufficient to maintain the patch in place on the skin for the recommended treatment period while allowing the patch to be readily removed without causing skin irritation or leaving adhesive residue on the skin.

EP-A-0 346 211 describes the use of a copolymer of 2-ethyl-hexyl acrylate and N-vinyl-2-pyrrolidone without absorption promoters. EP-A-0 272 918 describes the use of a macroporous foam in which active ingredient is present in immobilized form. EP-A-0 409 383 describes an estrogen-containing patch in the concentration range from 0.01 to 1% of an estrogen in combination with a water-insoluble vinyl-pyrrolidone for retarded release of the active ingredient to the skin.

U.S. Patent No. 4,994,267 describes a mixture of a synthetic or natural rubber in combination with an ethylene/vinyl acetate copolymer and acrylate. AU-A-91.76 582 (JP SN 90.202 409) describes the use of an acrylate adhesive in combination with a polyester carrier film. EP-A-0 416 842 describes the use of acrylate copolymers without absorption promoters, which contain active ingredients, preferably oestrogens or norethisterone or norethisterone acetate, by themselves or in combination. These above-described patches are merely carriers of drugs, which allow no control over absorption. Multilayer structured patches are relatively thick, and are therefore fairly uncomfortable on the skin. Furthermore, their appearance and their thickness do not enable the user to wear them in discreet manner.

It is desirable to provide a more aesthetically pleasing, more comfortable, and less obtrusive topical patch for delivering cosmetic, dermatological, and pharmaceutical active ingredients into the skin which may be applied to sensitive skin sites, such as around the eye.

Summary of the Invention

The present invention provides a patch comprising a bioadhesive water soluble polymeric matrix for delivering cosmetic, dermatological, and pharmaceutical active ingredients onto the skin, hair follicles, and sebaceous glands. The patch of the present invention provides ease of handling and application to the treatment site, comfort, and minimal foreign body sensation. Other preferred characteristics of the patch of the present invention include instantaneous adhesion to the surface upon application; increased residence time for the protection of the affected tissue or the delivery of the active ingredients; and ease of removal of the patch from the affected tissue or natural dissolution of the patch at the delivery site. The patch can further comprise a detachable protective layer to protect the patch from any external contamination during storage prior to use of the patch. Methods for treating the skin surfaces, hair follicles, and sebaceous glands, by applying the patch to the treatment site for the delivery cosmetic, dermatological, and pharmaceutical active ingredient, are also provided.

Detailed Description of the Invention

The present invention relates to a novel patch to deliver cosmetic, dermatological, and pharmaceutical active ingredients onto the skin, hair follicles, and sebaceous glands. The patch can be translucent or invisible. Upon application and adherence of the patch to the surface of skin, the cosmetic, dermatological, and pharmaceutical active ingredients, diffuse, or penetrate the surrounding tissues, and provide effective delivery to the treatment site. The patch of the present invention offers the advantages of an effective residence time with minimal discomfort and ease of use, and is an appropriate vehicle for local as well as systemic delivery of active ingredients.

Upon application, the patch adheres to the skin surface and holds in place. Water absorption softens the patch, diminishing and eliminating any foreign body sensation. As the patch rests on the skin, delivery of the active ingredients is provided. Residence times can vary, depending on the formulation and materials used. The residence times can be modulated between about a minute to about 24 hours. In addition to providing controlled delivery, once the patch adheres to the surface, it also provides protection to the treatment site, acting as an adhesive bandage. The dissolution rate of the patch in water can be adjusted by selection of polymers used in the patch.

In accordance with the teachings of the present invention the patch comprises bioadhesive film forming polymers. The film forming polymers can be water soluble. The use of water-soluble materials allows the removal of the patch from the skin by rinsing the site with water. Suitable water soluble film forming polymers include carbohydrates, such as starch derived from different plant sources, including high amylose and high amylopectin varieties. The term "starch," as referred to herein, is also meant to include water soluble film forming polymeric materials derived from starch including starch derivatives such as starch hydrolyzate products, modified starches, modified starch derivatives and maltodextrins. Other bioadhesive, water soluble polymers for use in the present invention are polyvinyl alcohol, cellulose and its derivatives, polysaccharide gums and their derivatives, polyethylene glycol, water soluble acrylics, water soluble polyesters, hydroxyalkyl starches, polyvinyl pyrrolidone, polyvinyl pyrrolidone cellulose derivatives, casein, gelatin, solubilized proteins, polyacrylamide, polyamines, polyquaternary amines, styrene maleic anhydride (SMA)

resins, polyethylene amine and any other conventional water soluble polymer or a combination thereof of the above-described materials. Combinations of different polymers or similar polymers with definite molecular weight characteristics can be used in order to achieve preferred film forming capabilities, mechanical properties, and kinetics of dissolution.

Solubilizers suitable for use in the present invention include glycerol, propylene glycol, polyalcohols, sorbitol and sorbitol derivatives.

The active substances to be released by the patch can serve the dermal treatment of local skin diseases, the intradermal and transdermal treatment of diseases, the treatment of wounds, or the skin care in cosmetic preparations.

The patch can include one or more cosmetic, dermatological, and pharmaceutical active ingredients that have an effect on the skin, including, but not limited to: anti-oxidants; free radical scavengers; moisturizers; depigmentation agents; reflectants; humectants; antimicrobial (e.g., antibacterial) agents; allergy inhibitors; anti-acne agents; anti-aging agents; anti-wrinkling agents, antiseptics; analgesics; antitussives; antipruritics; local anesthetics; anti-hair loss agents; hair growth promoting agents; hair growth inhibitor agents, antihistamines; keratolytic agents; anti-inflammatory agents; fresheners; healing agents; anti infectives; inflammation inhibitors; anticholinergics; vasoconstrictors; vasodilators; wound healing promoters; peptides, polypeptides and proteins; deodorants and antiperspirants; skin emollients and skin moisturizers; hair conditioners; hair softeners; hair moisturizers; tanning agents; skin lightening agents; antifungals such as antifungals for foot preparations; depilating agents; external analgesics; counterirritants; hemorrhoidals; insecticides; poison ivy products; poison oak products; burn products; anti-diaper rash agents; prickly heat agents; make-up preparations; vitamins; amino acids and their derivatives; herbal extracts; retinoids; flavoids; sensory markers (i.e., cooling agents, heating agents, etc.); skin conditioners; hair lighteners; chelating agents; cell turnover enhancers; coloring agents; sunscreens; anesthetics; immunomodulators and nourishing agents; moisture absorbers; sebum absorbers and the like, and mixtures thereof.

Local anaesthetics, local antibiotics, antiseptics, antimycotics, antihistaminics, and antipruritic drugs; keratolytics and caustic drugs; virustatics, antiscabietic agents,

steroids, as well as different substances for the treatment of acne, psoriasis, photodermatoses, or precancerous stages can be used with the patch of the present invention for the dermal treatment of local skin diseases. Active substances applicable by the intradermal route with the patch of the present invention include, for example, steroid and non-steroid antirheumatics, local anaesthetics, substances stimulating the blood flow, vasoprotectors and vasoconstrictors to treat vascular diseases, as well as active substances to influence processes in the subcutaneous fatty tissue. Transdermally applicable active substances to be used in the patch of the present invention include, for example, analgesics, anti-arrhythmic drugs, narcotics and their antagonists, neuroleptics, hormones or hormone substitutes, antidepressants, tranquilizers, hypnotics, psychostimulants, antiparkinson drugs, ganglionic blockers, sympathomimetics, alpha-sympatholytics, beta-sympatholytics, antisympathotonics, anti-asthmatics, antiemetics, appetite depressants, diuretics, or active substances for weight reduction, and the like. Because of the small thickness of the system according to the present invention preferred active substances are those developing their action already at very low concentrations. Examples of these preferred active substances include steroids, such as estradiol, estriol, progesterone, norethisterone, norethindrone, levonorgestrel and their derivatives, as well as estradiol diacetate, norgestamate, gestagens, desogestrel, demegestrone, promegestrone, testosterone, hydrocortisones and their derivatives; nitro compounds, such as amyl nitrate, nitroglycerin, isosorbide dinitrate; amine compounds, such as nicotine, chlorpheniramine, terfenadine, and triprolidine; oxicam derivatives such as piroxicam; mucopolysaccharases such as thiomucase; opioid substances such as buprenorphine, morphine, fentanyl and their salts, derivatives or analogues, naloxone, codeine, dihydroergotamine, lysergic acid derivatives, pizotiline, salbutamol, terbutaline; prostaglandins, such as PGA, PGB, PGE and the PGF-series, for example, misoprostol and enprostil, omeprazol, imipramine; benzamides, such as metoclopramines and scopolamine; peptides and growth factors such as EGF, TGF, PDGF, and the like; somatostatin; clonidin; dihydropyridines, such as nifedipine, nitrendipine, verapamil, diltiazem, ephedrine, propanolol, metoprolol, spironolactone; thiazides such as hydrochlorothiazide and flunarizine. Styptic active substances and wound-cleansing substances, such as enzymes, antiseptics, disinfectants, and antibiotics; pain-relieving

agents and anaesthetic active substances, as well as active substances promoting wound healing to stimulate granulation, to induce vascularization, or to promote epithelization can be used with the patch of the present invention for the treatment of wounds.

The patch of the present invention can also comprise a steroid hormone, preferably estradiol either alone or combined with other drugs, which is used in transdermal application for hormone substitution during postmenopause or for the treatment of osteoporosis. The patch of the present invention including estradiol can also be applied on long-term wounds, for instance crural ulcera, for the treatment of wounds.

The patch of the present invention can also comprise vegetable preparations, such as extracts or tinctures for the treatment of topical skin diseases. Suitable extracts or tinctures include oak bark extract, walnut extract, tincture of arnica, hamamelis extract, ribwort extract, pansy extract, thyme or sage extract; for the treatment of damaged or injured skin, for example, St. John's wort tincture, cone flowers tincture, chamomile flowers extract, or calendula flowers tincture; and for the care of exhausted and damaged skin, for example, birch leaves extract, nettle extract, coldsfoot extract, comfrey tincture, horsetail extract, or aloe vera extract. Vegetable preparations can also be released from the film layer for the intradermal treatment of diseases, for example, extracts of horse chestnut and butcher's broom in case of vein diseases, or extracts and tinctures of arnica, calendula, and capsicum in case of contusions, distortions, or haemorrhages. Vegetable preparations in the system according to the present invention may also be used in transdermal therapy, for example, ginseng extract in case of geriatric complaints; valerian tincture, extracts of melissa and hop to cause a sedative effect in case of superexcitation, sleep disturbances, and stress; extracts of kola and tea to achieve a stimulative effect; or hawthorn extract to stabilize the circulatory system.

Suitable effervescent agents that can be used with the patch of the present invention include sodium bicarbonate and sodium carbonate.

Suitable amino acid agents that can be used with the patch of the present invention include amino acids derived from the hydrolysis of various proteins as well as the salts, esters, and acyl derivatives thereof. Examples of such amino acid agents include amphoteric amino acids such as alkylamido alkylamines, stearyl acetyl glutamate, capryloyl silk amino acid, caprylol collagen amino acids; capryloyl kertain amino acids;

capryloyl pea amino acids; cocodimonium hydroxypropyl silk amino acids; corn gluten amino acids; cysteine; glutamic acid; glycine; hair keratin amino acids; hair amino acids such as aspartic acid, threonine, serine, glutamic acid, proline, glycine, alanine, half-cystine, valine, methionine, isoleucine, leucine, tyrosine, phenylalanine, cysteic acid, lysine, histidine, arginine, cysteine, tryptophan, citrulline; lysine; silk amino acids, wheat amino acids; and mixtures thereof

Suitable peptides, polypeptides, and proteins that can be used with the patch of the present invention include those polymers that have a long chain, such as at least about 10 carbon atoms, and a high molecular weight, such as at least about 1000, and are formed by self-condensation of amino acids. Examples of such proteins include collagen, deoxyribonuclease, iodized corn protein; keratin; milk protein; protease; serum protein; silk; sweet almond protein; wheat germ protein; wheat protein; wheat protein, alpha and beta helix of keratin proteins; hair proteins, such as intermediate filament proteins, high-sulfur proteins, ultrahigh-sulfur proteins, intermediate filament-associated proteins, high-tyrosine proteins, high-glycine tyrosine proteins, tricohyalin, and mixtures thereof.

Examples of suitable vitamins that can be used with the patch of the present invention include vitamin B complex; including thiamine, nicotinic acid, biotin, pantothenic acid, choline, riboflavin, vitamin B6, vitamin B12, pyridoxine, inositol, carnitine; vitamins A, C, D, E, K and their derivatives such as vitamin A palmitate and pro-vitamins, such as panthenol (pro vitamin B5) and panthenol triacetate, and mixtures thereof.

Examples of suitable antibacterial agents that can be used with the patch of the present invention include bacitracin, erythromycin, neomycin, tetracycline, chlortetracycline, benzethonium chloride, phenol, and mixtures thereof.

Examples of suitable skin emollients and skin moisturizers that can be used with the patch of the present invention include mineral oil, lanolin, vegetable oils, isostearyl isostearate, glyceryl laurate, methyl gluceth 10, methyl gluceth 20 chitosan, and mixtures thereof.

Examples of suitable hair conditioners that can be used with the patch of the present invention include quaternized compounds such as behenamidopropyl PG-dimonium chloride, tricetylammonium chloride, dihydrogenated tallowamidoethyl

hydroxyethylmonium methosulfate, and mixtures thereof as well as lipophilic compounds like cetyl alcohol, stearyl alcohol, hydrogenated polydecene, and mixtures thereof.

Examples of sunscreen agents that can be used with the patch of the present invention include butyl methoxydibenzoylmethane, octyl methoxycinnamate, oxybenzone, octocrylene, octyl salicylate, phenylbenzimidazole sulfonic acid, ethyl hydroxypropyl aminobenzoate, menthyl anthranilate, aminobenzoic acid, cinoxate, diethanolamine methoxycinnamate, glyceryl aminobenzoate, titanium dioxide, zinc oxide, oxybenzone, padimate o, red petrolatum, and mixtures thereof. An example of a suitable tanning agent that can be used with the patch of the present invention is dihydroxyacetone. Examples of suitable skin lightening agents that can be used with the patch of the present invention include hydroquinone, catechol and its derivatives, ascorbic acid and its derivatives, and mixtures thereof.

Examples of suitable insecticides that can be used with the patch of the present invention (including insect repellents, anti-scabies and anti-lice treatments) include permethrin, pyrethrin , piperonyl butoxide, imidacloprid, N,N-diethyl toluamide, which refers to the material containing predominantly the meta isomer.

An example of a suitable anti fungal for foot preparations that can be used with the patch of the present invention includes tolnaftate.

Examples of suitable depilating agents that can be used with the patch of the present invention include calcium thioglycolate, magnesium thioglycolate, potassium thioglycolate, strontium thioglycolate, and mixtures thereof.

Examples of suitable external analgesics and local anesthetics that can be used with the patch of the present invention include benzocaine, dibucaine, benzyl alcohol, camphor, capsaicin, capsicum, capsicum oleoresin, juniper tar, menthol, methyl nicotinate, methyl salicylate, phenol, resorcinol, turpentine oil, and mixtures thereof.

Examples of suitable antiperspirants and deodorants that can be used with the patch of the present invention include aluminium chlorohydrates, aluminium zirconium chlorohydrates, and mixtures thereof.

Examples of suitable counterirritants that can be used with the patch of the present invention include camphor, menthol, methyl salicylate, peppermint and clove oils, ichtammol, and mixtures thereof.

An example of a suitable inflammation inhibitor that can be used with the patch of the present invention includes hydrocortisone.

Examples of suitable hemorrhoidal products that can be used with the patch of the present invention include anesthetics such as benzocaine, pramoxine hydrochloride, and mixtures thereof; antiseptics such as benzethonium chloride; astringents such as zinc oxide, bismuth subgallate, balsam Peru, and mixtures thereof; skin protectants such as cod liver oil, vegetable oil, and mixtures thereof.

A type of benefit agent that can be used with the patch of the present invention includes those therapeutic agents that are effective in the treatment of dandruff, seborrheic dermatitis, and psoriasis as well as the symptoms associated therewith. Examples of such suitable therapeutic agents include zinc pyrithione, shale oil and derivatives thereof such as sulfonated shale oil, selenium sulfide, sulfur; salicylic acid; coal tar; povidone-iodine and imidazoles.

Antimicrobials that can be used with the patch of the present invention for topical application are penicillins, cephalosporins, other beta-lactam compounds, aminoglycosides, tetracyclines, erythromycin, antifungal agents, and the like and a combination thereof.

Antiseptics that can be used with the patch of the present invention for topical application onto acneiform skin are triclosan (Irgasan DP 300), phenoxy isopropanol, resorcinol, chlorhexidine, povidone and iodine.

Keratolytic agents that can be used with the patch of the present invention for topical application onto acneiform skin are salicylic acid, benzoyl peroxide, sulphur, retinoic acid and any of a number of fruit acids and alpha hydoxy acids.

Anti-irritants that can be used with the patch of the present invention for the topical application onto acneiform skin are alpha-bisabolol, farnesol, chamomile extract and glycyrrhetinic acid.

Examples of anti-inflammatory analgesic agents that can be used with the patch of the present invention include acetaminophen, methyl salicylate, monoglycol salicylate, aspirin, mefenamic acid, flufenamic acid, indomethacin, diclofenac, alclofenac, diclofenac sodium, ibuprofen, ketoprofen, naproxen, pranoprofen, fenoprofen, sulindac, fenclofenac, clidanac, flurbiprofen, fentiazac, bufexarnac, piroxicam, phenylbutazone,

oxyphenbutazone, clofezone, pentazocine, mepirizole, tiaramide hydrochloride, and the like. Examples of steroidal anti-inflammatory agents that can be used with the patch of the present invention include hydrocortisone, predonisolone, dexamethasone, triamcinolone acetonide, fluocinolone acetonide, hydrocortisone acetate, predonisolone acetate, methylpredonisolone, dexamethasone acetate, betamethasone, betamethasone valerate, flumetasone, fluorometholone, beclomethasone diproprionate, and the like.

Examples of antihistamines that can be used with the patch of the present invention include diphenhydramine hydrochloride, diphenhydramine salicylate, diphenhydramine, chlorpheniramine hydrochloride, chlorpheniramine maleate isothipendyl hydrochloride, tripelennamine hydrochloride, promethazine hydrochloride, methdilazine hydrochloride, and the like. Examples of local anesthetics that can be used with the patch of the present invention include dibucaine hydrochloride, dibucaine, lidocaine hydrochloride, lidocaine, benzocaine, p-buthylaminobenzoic acid 2-(die-ethylamino) ethyl ester hydrochloride, procaine hydrochloride, tetracaine, tetracaine hydrochloride, chloroprocaine hydrochloride, oxyprocaine hydrochloride, mepivacaine, cocaine hydrochloride, piperocaine hydrochloride, dyclonine, dyclonine hydrochloride, and the like.

Examples of bactericides and disinfectants that can be used with the patch of the present invention include thimerosal, phenol, thymol, benzalkonium chloride, benzethonium chloride, chlorhexidine, povidone iode, cetylpyridinium chloride, eugenol, trimethylammonium bromide, and the like. Examples of vasoconstrictors that can be used with the patch of the present invention include naphazoline nitrate, tetrahydrozoline hydrochloride, oxymetazoline hydrochloride, phenylephrine hydrochloride, tramazoline hydrochloride, and the like. Examples of hemostatics that can be used with the patch of the present invention include thrombin, phytonadione, protamine sulfate, aminocaproic acid, tranexamic acid, carbazochrome, carbaxochrome sodium sulfanate, rutin, hesperidin, and the like.

Examples of chemotherapeutic drugs that can be used with the patch of the present invention include sulfamine, sulfathiazole, sulfadiazine, homosulfamine, sulfisoxazole, sulfisomidine, sulfamethizole, nitrofurazone, and the like. Examples of antibiotics that can be used with the patch of the present invention include penicillin,

meticillin, oxacillin, cefalotin, cefalordin, erythromcycin, lincomycin, tetracycline, chlortetracycline, oxytetracycline, metacycline, chloramphenicol, kanamycin, streptomycin, gentamicin, bacitracin, cycloserine, and the like.

Examples of antiviral drugs that can be used with the patch of the present invention include protease inhibitors, thymadine kinase inhibitors, sugar or glycoprotein synthesis inhibitors, structural protein synthesis inhibitors, attachment and adsorption inhibitors, and nucleoside analogues such as acyclovir, penciclovir, valacyclovir, and ganciclovir.

Example of cosmetic active ingredients that can be used with the patch of the present invention are D-alpha-tocopherol, DL-alpha-tocopherol, D-alpha-tocopheryl acetate, DL-alpha-tocopheryl acetate, ascorbyl palmitate, vitamin F and vitamin F glycerides, vitamin D, vitamin D_2, vitamin D_3, retinol, retinol esters, retinyl palmitate, retinyl propionate, beta-carotene, D-panthenol, famesol, farnesyl acetate; jojoba oils and blackcurrant oils rich in essential fatty acids; 5-n-octanoylsalicylic acid and esters thereof, salicylic acid and esters thereof; alkyl esters of .alpha.-hydroxy acids such as citric acid, lactic acid, glycolic acid; asiatic acid, madecassic acid, asiaticoside, total extract of Centella asiatica, beta-glycyrrhetinic acid, alpha-bisabolol, ceramides such as 2-oleoylamino- 1,3-octadecane; phytanetriol, phospholipids of marine origin which are rich in polyunsaturated essential fatty acids, ethoxyquine; extract of rosemary, extract of balm, quercetin, extract of dried microalgae, anti-inflammatory agents, such as steroidal anti-inflammatory agents, and biostimulants, for example hormones or compounds for the synthesis of lipids and/or proteins.

Alpha-Hydroxy acids (AHAs) can be used in the patch of the present invention as exfoliants, moisturizers, and emollients. Lactic acid salts can be used in the patch of the present invention such as sodium lactate, and can be hypothesized to be part of the skin's own natural moisturizing system. In addition, AHAs and salicylic acid can be used in the patch of the present invention as a structurally similar beta-hydroxy acid as peeling agents. The moisturizing activity of AHAs and their ability to exfoliate the skin and interfere with intercellular cohesion in the outer epidermis is well known. It has been suggested that AHAs interfere with cohesion in the stratum granulosum, unlike salicylic acid and other exfoliants.

Vitamin C (ascorbic acid) can be used in the patch of the present invention. Vitamin C promotes collagen (connective tissue) synthesis, lipid (fat) and carbohydrate metabolism, and the synthesis of neurotransmitters. It is also essential for optimum maintenance of the immune system. Vitamin C is toxic to a wide range of cancer cells, especially melanoma. The oxidizing enzyme tyrosine that catalyzes the aerobic action of tyrosine into melanin and other pigments is also inhibited by the presence of vitamin C. Vitamin C has been found to be effective in catalyzing the immune response to many viral and bacterial infections. Besides the many applicable uses set forth above, vitamin C is essential for collagen synthesis and wound healing. The patch of the present invention can comprise a combination of vitamin C, vitamin E and other ingredients, such as moisturizers, collagen synthesis promoting agents and exfoliating agents.

Skin treating compositions can be used in the patch of the present invention. Skin treating compositions can comprise vitamin C, vitamin E, and optionally, alpha-hydroxy acids, such as lactic and glycolic acids and other keratinolytics for the treatment or prevention of wrinkles and skin dryness.

According to the present invention the patch can also be marked in the form of colors, letters, numbers, dates, codes, pictographs and the like by means of screen printing. The film layer of the patch can be dyed by means of soluble dyes or pigments. Alternatively, the patch can be completely transparent or invisible on the skin.

Skin conditioners, moisturizers and surfactants can be included as additives in the patch of the present invention. Illustrative conditioners include mineral oil, petrolatum, vegetable oils (such as soybean or maleated soybean oil), dimethicone, dimethicone copolyol, cationic monomers and polymers (such as guar hydroxypropyl trimonium chloride and distearyl dimethyl ammonium chloride) as well as combinations thereof. Illustrative moisturizers are polyols such as sorbitol, glycerin, propylene glycol, ethylene glycol, polyethylene glycol, polypropylene glycol, 1,3-butane diol, hexylene glycol, isoprene glycol, xylitol, fructose and mixtures thereof.

Surfactants can be used in the patch of the present invention such as those selected from the anionic, cationic, nonionic, amphoteric, zwitterionic and combinations thereof. Most preferred are nonionic and amphoteric surfactants due to their mildness. Examples of suitable amphoterics are cocoamidopropylbetaine and lauroamphoacetate.

Examples of suitable nonionics are dialkylamine oxides, alkyl polyglycosides and methyl glucamides. Examples of mild anionic surfactants include salts of sarcosinate, taurate and cocoyl isethionate. Other surfactants that can be used in the patch of the present invention are sucrose distearate, diglyceryldistearate, tetraglyceryl tristearate, decaglyceryl decastearate, diglyceryl monostearate, hexaglyceyl tristearate, decaglyceryl pentastearate, sorbitan monostearate, sorbitan tristearate, diethylene glycol monostearate, the ester of glycerol and of palmitic acid and stearic acid, monostearate polyoxyethylenated with 2 OE (containing 2 oxyethylene units), glyceryl mono- and dibehenate and pentaerythrityl tetrastearate.

The amount of conditioners, moisturizers and surfactants used in the patch of the present invention can each independently range from about 0.01 to about 45%, preferably from about 0.1 to about 30%, most preferably from about 1 to about 20% by weight for each category.

The concentration of the active ingredient in the patch of the present invention depends on the desired treatment strength. Typically, this concentration can range from about 0.001% to about 80% by weight relative to the total weight of the oily phase. Preferably, this percentage is in the range of about 1% to about 50%.

Plasticizers, penetration enhancer, as described in the text "Transdermal Delivery of Drugs, A. F. Kydonieus (ED) 1987 CRL Press and in U.S. Pat. Nos. 4,913,905, 4,917,676 and 5,032,403 hereby incorporated by reference into this application, coloring agents, and preservatives can be included in the patch of the present invention and comprise no more than about 10% of the final weight of the patch, but the amount can vary depending on the active ingredient or other components. Glycerin, which is also a moisturizing agent, can be added as an anti-irritant or to modulate the delivery of the other skin treating agents and can be present in amounts of from about 0 to about 20% by weight.

The patch of the present invention can be prepared by numerous methods known in the art. In one embodiment, the components are dissolved in an appropriate solvent or combination of solvents to prepare a solution. Solvents for use in the present invention comprise water, methanol, ethanol, or low alkyl alcohols such as isopropyl alcohol, acetone, or dichloroethane, alone or combination. The solvent can also be used as a

plasticizer or dissolution-rate-modifying agent. The patch may consist of a detachable protective layer to protect the patch from any external contamination during storage prior to use of the patch.

The patch of the present invention can be applied to human skin using hands by wetting the patch or the targeted site. The patch becomes tacky when wetted, and adheres onto the skin. The adhesive properties of the patch are sufficient to maintain the patch in place on the skin for the recommended treatment period while allowing the patch to be readily removed without causing skin irritation or leaving adhesive residue on the skin. The patch can be removed by rinsing the area with water, thus requiring less force than other conventional pressure-sensitive adhesive patches.

The patch of the present invention can include a detachable protective layer to protect the patch from external contamination during storage prior to use of the patch. The protective layer can be formed of plastic or paper.

The patch of the invention can also contain encapsulated active ingredients in water sensitive or hydrophobic controlled release systems in the form of nanospheres and microspheres. The encapsulated active ingredients are dispersed homogeneously in the polymeric film. Examples of encapsulated active ingredients in water sensitive microspheres are spray dried active ingredients with starch and other natural or synthetic water-soluble polymers. On contact with skin moisture, the spray dried microspheres, comprising the active ingredients, are released, thereby promoting the controlled delivery or the enhanced bioavailability of active ingredients and minimizing the interaction of active ingredients with the other compounds present in the patch. Examples of encapsulated ingredients in nanospheres are dispersions of hydrophobic materials, such as lipids, waxes, and hydrophobic polymers comprising active ingredients in the hydrophobic matrix. On contact with skin moisture, the hydrophobic nanospheres, comprising the active ingredients, are released, thereby promoting the controlled delivery or the enhanced bioavailability of active ingredients and minimizing the interaction of active ingredients with the other compounds present in the patch.

The primary active ingredients to be delivered to the skin are preferably cosmetic, dermatological, and pharmaceutical and can be a single agent or can comprise a mixture of active ingredients.

In order to ensure that the patch is simple and comfortable to use, a suitable size and thickness of a single patch has been identified. The patch of the present invention can be produced in a variety of sizes dependent on the area to be treated. The size of the patch is classified as a small patch being about 0.5 to about 2 cm^2 and a large patch up to about 40 cm^2. Typically, the size of the patch is from about 0.5 to about 3 cm^2 and preferably about 2 cm^2. The patch can be made in a variety of shapes and can be substantially transparent or clear, a flesh-like color or shade so as to effectively blend with the skin of wearer and appears invisible or translucent. The patches according to the present invention can be cut according to an appropriate contour corresponding to the region of skin surface to be treated, for example in the form of a mask for application to the face, especially for application around the eyes, on the bags under the eyes or on the forehead. The patch according to the present invention can be cut into any other shape required for application to a defined region of the body. In general, the size of a patch in accordance with the invention is between about 0.25 cm^2 to about 500 cm^2. A patch intended for the depigmentation of pigmented skin blemishes can be small in size, less than about 1 cm^2. For example, a patch with a slimming action can have a large surface area, which is sufficient to cover part of a thigh. The patches cut to a desired size and shape can be used on a surface of skin to be treated by applying them directly to the skin after the targeted area has been wetted.

The thickness of the patch can have a range from about 10 microns to about 1000 microns, and more preferably from about 50 to about 250 microns.

The invention also provides a method for the use of the patch to deliver agents to the skin. The method generally comprises wetting the patch, or the target surface and applying the patch to the skin. The patch can be removed from the skin by washing the area with water.

The invention can be further illustrated by the following examples preferred embodiments thereof, although it will be understood that these examples are included merely for purposes of illustration and are not intended to limit the scope of the invention unless otherwise specifically indicated. All percentages, ratios, and parts herein, in the Specification, Examples, and Claims, are by weight and are approximations unless otherwise stated.

EXAMPLES

EXAMPLE 1

Preparation of a patch for acne treatment

Compositions used in the preparation of a patch for the topical treatment of acne and acnei form skin diseases are described in Table 1-4. The examples were conducted using salicylic acid, as keratolytic agent, in an amount of 0.1 to 2% w/w together with an anti-irritant such as alpha-bisabolol in 0.01 to 3% w/w, an antiseptic such as triclosan (Irgasan DP 300) in 0.1 to 1% w/w, ascorbic acid (Vitamin C), vitamin E, and a solubilizer such as sorbitan monooleate in 0.1 to 5% w/w. Both ascorbic acid and vitamin E are useful in the topical treatment of acne.

TABLE 1

COMPONENT	QUANTITY % w/w (on a dry basis)
Hydroxypropyl Cellulose	96.5
alpha-Bisabolol[1]	1.0
Irgasan DP 300[2]	0.3
Salicylic acid	0.2
sorbitan monooleate	2

[1]alpha-Bisabolol is 6-methyl-2-(4-methyl-3-cyclohexen-1-yl)-5-hepten-2-ol
[2]Irgasan DP 300 is 2,4,4'-trichloro-2'-hydroxy diphenyl ether

TABLE 2

COMPONENT	QUANTITY % w/w (on a dry basis)
Hydroxypropyl Cellulose	84.8
Salicylic acid	0.2
Ascorbic Acid	10
Spray dried particles of Vitamin E	5

TABLE 3

COMPONENT	QUANTITY % w/w (on a dry basis)
Polyvinyl Alcohol	65.8
Polyvinyl Pyrrolidone	15
Glycerin	4
Salicylic acid	0.2
Ascorbic Acid	10
Vitamin E	5

TABLE 4

COMPONENT	QUANTITY % w/w (on a dry basis)
Gantrez®[1] S-97 BF	
Glycerin	4
Salicylic acid	0.2
Ascorbic Acid	10
Vitamin E	5
Green Tea Extract	5

[1] Gantrez® S-97 BF is 2-Buttenedioic Acid (Z)-, Polymer with Methoxyethene (commercially available from the ISP Technologies, Inc. of Wayne, New Jersey)

The patch was cut into a circular shape with nominal size of 1 cm^2 and thickness of 150 microns. The target area on the skin was wetted and the patch was applied.

EXAMPLE 2

Preparation of a patch for skin lightening

Compositions used in the preparation of a patch for skin lightening that contains an inhibitor of tyrosinase activity, phytolight®, as skin lightening agent (a mixture of botanical extracts, Coletica Inc., Northport New-York) are described in Table 5-6.

TABLE 5

COMPONENT	QUANTITY % w/w (on a dry basis)
Hydroxypropyl Cellulose	85
phytolight®	5
Ascorbic Acid	5
Vitamin E	5

TABLE 6

COMPONENT	QUANTITY % w/w (on a dry basis)
Polyvinyl Alcohol	80
Polyvinyl Pyrrolidone	10
phytolight®	5
Ascorbic Acid	5

The patch was cut into a circular shape with nominal size of 1 cm^2 and thickness of 150 microns. The target area on the skin was wetted and the patch was applied.

EXAMPLE 3

Preparation of a patch to reduce eye puffiness

Compositions used in the preparation of a patch to reduce eye puffiness that contains a stabilized flavonoid extract that stimulate blood circulation and inhibits elastase, flavagrum® PEG, as active agent (a mixture of botanical extracts, Coletica Inc., Northport New-York) are described in Table 7-8.

TABLE 7

COMPONENT	QUANTITY % w/w (on a dry basis)
Hydroxypropyl Cellulose	95
flavagrum® PEG	5

TABLE 8

COMPONENT	QUANTITY % w/w (on a dry basis)
Polyvinyl Alcohol	80
Polyvinyl Pyrrolidone	14
flavagrum® PEG	5
cooling agent[1]	1

[1]Cyclohexanecarboxamide, N-Ethyl-5-Methyl-2-(1-Methylethyl)-

The patch was cut into a circular shape with nominal size of 1 cm^2 and thickness of 150 microns. The target area on the skin was wetted and the patch was applied.

EXAMPLE 4

Preparation of a depilatory patch

Compositions used in the preparation of hair removal are described in Table 9-11. The examples are conducted using Calcium Thioglycolate or Potassium Thioglycolate as depilatory agents, in an amount of 5 to 20% w/w together with calcium hydroxide or sodium hydroxide in 1 to 10% w/w, Urea as hair swelling agent in 4 to 10% w/w, and Glycerin as plasticizer at 1 to 20% w/w.

TABLE 9

COMPONENT	QUANTITY % w/w (on a dry basis)
Hydroxypropyl Cellulose	88
Urea	4
Sodium Hydroxide	2
Potassium Thioglycolate	6

TABLE 10

COMPONENT	QUANTITY % w/w (on a dry basis)
Polyvinyl Alcohol	60
Polyvinyl Pyrrolidone	14
Glycerin	10
Calcium Thioglycolate	10
Calcium Hydroxide	2
Urea	4

TABLE 11

COMPONENT	QUANTITY % w/w (on a dry basis)
Polyvinyl Alcohol	30
Polyvinyl Pyrrolidone	10
Glycerin	15
Calcium Thioglycolate	15
Calcium Hydroxide	5
Urea	4
Fragrance	1

The patch was cut into a circular shape with nominal size of 1 cm^2 and thickness of 150 microns. The depilatory patch is applied on the skin surface after wetting the area. The patch is allowed to stand for about 5 to 10 minutes and the strength of hair is reduced or dissolved by the effect of the depilatory agent. Hair can be removed without leaving any residue by washing off the patch from the skin.

EXAMPLE 5

Preparation of a patch for treating the signs of aging

Compositions used in the preparation of a patch for the topical treatment of skin to reduce the signs of aging are described in Table 12-14. The examples were conducted using anti aging and anti oxidants active ingredients such as retinol, ascorbic acid (Vitamin C), Vitamin E, Green Tea Extract.

TABLE 12

COMPONENT	QUANTITY % w/w (on a dry basis)
Instant Textra™[1]	75
Maltrin™ M100[2]	10
Glycerin	5
Ascorbic acid	10

[1]Instant Textra™ is a food starch-modified (commercially available from the National Starch and Chemical Company of Bridgewater, New Jersey)
[2]Maltrin™ M100 (commercially available from the Grain Processing Corporation of Muscatine, Iowa)

TABLE 13

COMPONENT	QUANTITY % w/w (on a dry basis)
N-Lite® L[1]	65
Maltrin™ M100[2]	10
Glycerin	5
Ascorbic acid	10
Green Tea Extract	10

[1] N-Lite® L is a food starch-modified (commercially available from the National Starch and Chemical Company of Bridgewater, New Jersey)
[2]Maltrin™ M100 (commercially available from the Grain Processing Corporation of Muscatine, Iowa)

TABLE 14

COMPONENT	QUANTITY % w/w (on a dry basis)
Instant Pure-Cote® B792[1]	65
Maltrin™ M100[2]	10
Glycerin	5
Ascorbic acid	10
Vitamin E	5

[1]Instant Pure-Cote® B792 is a food starch-modified (commercially available from the Grain Processing Corporation of Muscatine, Iowa)
[2]Maltrin™ M100 (commercially available from the Grain Processing Corporation of Muscatine, Iowa)

TABLE 15

COMPONENT	QUANTITY % w/w (on a dry basis)
Polyvinyl Alcohol	70
Polyvinyl Pyrrolidone	15
Glycerin	5
Retinol	10

The patch was cut into a circular shape with nominal size of 1 cm^2 and thickness of 150 microns. The target area on the skin was wetted and the patch was applied.

EXAMPLE 6

Preparation of a patch for burn treatment

Compositions used in the preparation of a local anesthetic patch to alleviate pain and discomfort are described in Table 16. The example is conducted using benzocaine.

TABLE 16

COMPONENT	QUANTITY % w/w (on a dry basis)
Polyvinyl Alcohol	70
Polyvinyl Pyrrolidone	15
Glycerin	10
Benzocaine[1]	1.5

[1]Benzocaine is ethyl 4-aminobenzoate

The benzocaine is a local anesthetic which would alleviate pain and discomfort, and Glycerin is an excellent humectant which moisturizes the skin. The patch was cut into a

circular shape with nominal size of 1 cm^2 and thickness of 150 microns. The target area on the skin was wetted and the patch was applied.

EXAMPLE 7

Preparation of a pain relief patch

Composition used in the preparation of a pain relief patch is described in Table 17. The example is conducted using ibuprofen.

TABLE 17

COMPONENT	QUANTITY % w/w (on a dry basis)
Polyvinyl Alcohol	70
Polyvinyl Pyrrolidone	15
Glycerin	10
ibuprofen	5

The patch was cut into a circular shape with nominal size of 1 cm^2 and thickness of 150 microns. The target area on the skin was wetted and the patch was applied.

EXAMPLE 8

Preparation of an antibiotic patch

Composition used in the preparation of an antibiotic patch to is described in Table 18. The example is conducted using chloramphenicol.

TABLE 18

COMPONENT	QUANTITY % w/w (on a dry basis)
Polyvinyl Alcohol	70
Polyvinyl Pyrrolidone	1
Glycerin	10
chloramphenicol	0.55

The patch is useful in the antibiotic treatment of a variety of topical bacterial, chlamydial, and rickettsial infections.

EXAMPLE 9

Preparation of self tanning patch

Composition used in the preparation of a self tanning patch to is described in Table 18. The example is conducted using dihydroxyacetone as tanning agent and L-Lysine as tanning accelerator.

TABLE 18

COMPONENT	QUANTITY % w/w (on a dry basis)
Polyvinyl Alcohol	70
Polyvinyl Pyrrolidone	15
Glycerin	5
dihydroxyacetone	5
L-Lysine	5

It is to be understood that the above-described embodiments are illustrative of only a few of the many possible specific embodiments which can represent applications of the principles of the invention. Numerous and varied other arrangements can be readily devised in accordance with these principles by those skilled in the art without departing from the spirit and scope of the invention.